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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,684	06/06/2005	Kathleen Grace Mountjoy	BSWV-P01-007	3069

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BORGEEST, CHRISTINA M	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,684	MOUNTJOY ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,11,15-20,23,25,29,30,32,33,35 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9,11,15-20,23,25,29,30,32,33,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed 21 February 2008 is acknowledged. Claims 8-9, 11, 15-18, 20, 23, 25 and 35 are amended. Claim 36 is new. Claims 10, 12-14, 21-22, 26-28, 31 and 34 are cancelled. Claims 8-9, 11, 15-20, 23, 25, 29, 30, 32, 33, 35 and 36 are under examination.

Rejections Withdrawn

Rejections made over claims 10, 21-22, 26-28 and 31 in the Office action mailed 29 October 2007 are hereby withdrawn in response to Applicants' cancellation of those claims.

In addition, the rejection of claim 9 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in part. Claim is included in the scope of enablement rejection discussed below.

Rejection maintained

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 8-9, 11, 15-20, 23, 25, 29, 30, 32 and 33 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained. In addition new claim 36 is hereby included in this rejection. Furthermore, claim 35 was inadvertently left of the list of rejected claims in the previous Office action (mailed 21 February 2008) due to typographical error (the Examiner typed 34, which had been cancelled, instead of 35).

Claims 8-9, 11, 15-20, 23, 25, 29, 30, 32, 33, 35 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assessing feeding and/or weight gain pattern or diagnosing obesity in an individual in need thereof, comprising measurement of α-MSH and desacetyl-α-MSH in a sample, calculating the ratio between desacetyl-α-MSH and α-MSH, and comparing the value of the ratio with a reference value, wherein a higher desacetyl-α-MSH/α-MSH ratio in the sample is indicative of an increase in feeding and/or weight gain and/or obesity, does not reasonably provide enablement for the claims as broadly recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicants argue at p. 7-9 that they are enabled for "sample", and in the Examiner's opinion, Applicants have provided adequate evidence that "sample" is enabled, given the evidence submitted in the form of Exhibits C-F.

Applicants argue that regarding "predicting" or "assessing" risk at p. 9-10, that the Examiner has based the enablement argument only on the basis of the presence or absence of working examples.

Applicants' argument has been fully considered but is not found persuasive. Even given the amendment, the claims still encompass predicting or assessing risk, which means the claims encompass predicting risk in a normal population. Applicants are not enabled for predicting or assessing risk. Looking at Applicants own working examples, non-obese (lean) mice were used as a control. If the claimed method is capable of predicting risk of obesity, then one should find that a certain percentage of the "normal" population test positive because a certain percentage of currently lean individuals are at risk for becoming overweight. Thus a test that predicts risk should identify those individuals who are currently normal but are at risk for developing obesity. In other words, it is not clear why some of the controls did not test positive. Because the working example only teaches an increase in the desacetyl-alpha-MSH/alpha- MSH ratio in ***already obese*** mice, but not lean mice, the claimed methods cannot be said to predict risk. Applicants' argument that the Examiner has based the enablement argument only on the basis of the presence/absence of working examples is not true. The Examiner based this argument on the results of the working example, which teaches that individuals who are already obese (thus do not require that their risk be predicted) tested positive and "normal" individuals (who are in need of predicting risk) all tested negative. For this reason, the claims are only enabled for assessing an increase in feeding and/or weight gain pattern in an individual who is already obese. If the test were truly predictive, then there should be some individuals testing positive in changes in the control group.

Applicants present arguments at p. 10-11 to address the Examiner's alleged assertion of "in vitro/in vivo correlation". Because the Examiner made no such arguments, this argument is misplaced.

Applicants present arguments regarding "imbalance" and "disturbance" pages 11-14. They argue that it is unclear how the Examiner can reach the conclusion that biochemical markers of feeding behavior is evident once the condition is manifested based on the data in Nakahara because this study "was not designed to address this question."

For the record, Nakahara measured obestatin in a group of obese patients and a group of anorexic patients, and compared the levels to control patients and found that obese patients have lower obestatin levels compared to control patients, while anorexic patients have higher obestatin levels compared to control patients. Additionally, as explained above, Applicants' own data teach that there is an increase in the desacetyl-alpha-MSH/alpha- MSH ratio in ***already obese*** mice, but not lean mice, thus it is still not clear how their method can be said to be capable of predicting risk. If the claimed methods predict risk of obesity, then they should be able to discern risk in a normal population, not just an obese one.

Furthermore, Applicants' arguments do not address the breadth of the terms such as "imbalance" and "disturbance" and "energy homeostasis". Imbalance and disturbance encompass underfeeding and weight loss, but the specification teaches that an increase in the desacetyl-α-MSH/α-MSH ratio is seen in obese mice, thus the claims are only enabled for assessing an increase in feeding and/or weight gain pattern in an individual who is already obese. An increase in the desacetyl-α-MSH/α-MSH ratio was only shown to diagnose obesity in already obese subjects, so to claim that such a method can "diagnose an imbalance in energy homeostasis" (see for example claim 11,

15, 16 and dependents) goes far beyond the reach of Applicants' own data. Furthermore, it unfairly requires the skilled artisan to determine the nature of the imbalance in energy homeostasis that is encompassed by the claims. As stated above, "imbalance" encompasses underfeeding, which the data do not address, and "energy homeostasis" encompasses maintenance of all bodily functions (for example, core body temperature, energy levels during exercise), which the data certainly do not address. The skilled artisan would be required to determine the nature of the imbalance or disturbance and types of energy homestasis that are encompassed by the claims, and could be unfairly limited from conducting research into such topics by the breadth of the claims.

Applicants submit references to rebut the Examiner's conclusion that Applicants' data teach that the biochemical marker of an increase in the desacetyl-α-MSH/α-MSH ratio become evident only as the condition manifest itself in the subject:

- The ratio of LDL/HDL has been used in the art as a predictor of future cardiovascular disease risk in a normal subject (see Jukema et al., Curr Med Res Opin. 21 (11): 1865-1874, 2005, Exhibit G).
- Another study suggests that the ratio of apolipoprotein (apo) B/apoAI is a better index for risk assessment of coronary artery disease (Rasouli et al., Clin Chem Lab Med. 44(8): 1015, 2006, Exhibit H)
- A study of neuroblastoma (Sandler et al., J Pediatr Surg. 37(3): 507-11, 2002, Exhibit I), it was found that the survivin/Fas ratio in primary tumors may be used to predict the risk for recurrent disease in patients with neuroblastoma
- A study investigated the role of serum C-reactive protein level was as a risk factor in predicting metabolic syndrome (MS), hypertension, atherogenic dyslipidemia, type 2 diabetes mellitus and coronary heart disease, which showed that elevated levels of C- reactive protein is both an independent significant predictor and a risk factor of cardiometabolic risk pertaining to MS, hypertension, atherogenic dyslipidemia, diabetes and coronary heart disease. (Onat et al., Metabolism Clinical and Experimental 57: 207-214, 2008, Exhibit J)

Finally, Applicant argues that Yarnell (cited by the Examiner) also contradicts the Examiner's position by showing that BMI index at age 18 is predictive of future obesity in middle age.

This argument has been fully considered but is not found persuasive. First, Applicants' argument and the presentation of other studies do nothing to explain the lack of ability of the currently claimed methods to predict risk of obesity in a lean (non-obese) population. If the claimed method is capable of predicting risk of obesity, then one should find that a certain percentage of the "normal" population test positive because a certain percentage of currently lean individuals are at risk for becoming overweight. Thus a test that predicts risk should identify those individuals who are currently normal but are at risk for developing obesity. In other words, it is not clear why some of the controls did not test positive. Because the working example only teaches an increase in the desacetyl-alpha-MSH/alpha- MSH ratio in ***already obese*** mice, but not lean mice, the claimed methods cannot be said to predict risk. If the test were truly predictive, then there should be some individuals testing positive in the control group. Second, even in the cited references, the populations who test positive already have the condition. For example, those individuals with abnormal LDL/HDL levels already exhibit the early stages of heart disease. Finally, regarding the study by Yarnell et al., on the contrary, this study perfectly illustrates the Examiner's point. The method (BMI measurment) was only predictive in individuals who already had high BMIs, i.e,. those individuals who were ***already obese***, which is similar to Applicants' working example. Again, a method which is truly predictive would be capable of predicting obesity in a normal population, since a certain percentage of normal individuals are at risk for developing obesity.

Finally Applicants argue at p. 13, last full paragraph that they "disagree with the Examiner's argument based on Yarnell. For one thing, Yamell have not assessed and compared the instant claimed invention to the other obesity prognostic factors, and thus cannot be logically relied upon to show that the BMI index method is superior than the claimed invention. Further more, even assuming for the sake of argument that the BMI method is the most accurate predictor, it does not necessarily follow that no other methods can be accurate. The Examiner appears to argue for the untenable position that only the best method works, while all others cannot."

Applicants' arguments have been fully considered but are not found persuasive. First, this argument bears special mention, because Applicants have inaccurately characterized the Examiner's words, since for the record, the Examiner never made such arguments with regard to the "superiority" of any methods. Contrary to Applicants' arguments regarding what the Examiner "appears" to have said, the Examiner ***actually*** said that Applicants own results teach an increase in the desacetyl-alpha-MSH/alpha-MSH ratio in ***already obese*** mice, but not lean mice, therefore the claimed methods cannot be said to predict risk. If the test were truly predictive, then there should be some individuals testing positive in the control group. Again, a method which is truly predictive would be capable of predicting obesity in a normal population, since a certain percentage of normal individuals are at risk for developing obesity. The Examiner has no thoughts as to the superiority of any methods, taught by Yarnell or others.

Finally, in general, the observation of one molecule being increased (i.e, an increase in desacetyl-alpha-MSH relative to alpha-MSH) in a diseased population can also be due to that molecule's production *as a result* of the condition, and thus the skilled artisan would not presume that the molecule could also be used to *predict* the disease or disorder unless it were shown that the molecule increased before symptom

onset. The data presented by Applicants suggest such a scenario, i.e., one in which an increase in desacetyl-alpha-MSH relative to alpha-MSH occurs as a result of the condition.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is (571)272-4482. The examiner can normally be reached on 8:00am - 2:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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